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NOTICE OF ALLOWANCE AND FEE(S) DUE

10

20350 7590 07/17/2003

TOWNSEND AND TOWNSEND AND CREW, LLP
TWO EMBARCADERO CENTER
EIGHTH FLOOR
SAN FRANCISCO, CA 94111-3834

EXAMINER

LEARY, LOUISE N

ART UNIT

CLASS-SUBCLASS

1654

435-004000

DATE MAILED: 07/17/2003

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/553,424	04/19/2000	Luke V. Schneider	020444-000400US	3984

TITLE OF INVENTION: METHODS FOR CONDUCTING METABOLIC ANALYSES

APPLN. TYPE	SMALL ENTITY	ISSUE FEE	PUBLICATION FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	YES	\$650	\$0	\$650	10/17/2003

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. **PROSECUTION ON THE MERITS IS CLOSED.** THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN **THREE MONTHS** FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. **THIS STATUTORY PERIOD CANNOT BE EXTENDED.** SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE REFLECTS A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE APPLIED IN THIS APPLICATION. THE PTOL-85B (OR AN EQUIVALENT) MUST BE RETURNED WITHIN THIS PERIOD EVEN IF NO FEE IS DUE OR THE APPLICATION WILL BE REGARDED AS ABANDONED.

HOW TO REPLY TO THIS NOTICE:

I. Review the SMALL ENTITY status shown above.

If the SMALL ENTITY is shown as YES, verify your current SMALL ENTITY status:

- A. If the status is the same, pay the TOTAL FEE(S) DUE shown above.
- B. If the status is changed, pay the PUBLICATION FEE (if required) and twice the amount of the ISSUE FEE shown above and notify the United States Patent and Trademark Office of the change in status, or

If the SMALL ENTITY is shown as NO:

- A. Pay TOTAL FEE(S) DUE shown above, or
- B. If applicant claimed SMALL ENTITY status before, or is now claiming SMALL ENTITY status, check the box below and enclose the PUBLICATION FEE and 1/2 the ISSUE FEE shown above.
- ☐ Applicant claims SMALL ENTITY status.
See 37 CFR 1.27.

II. PART B - FEE(S) TRANSMITTAL should be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). Even if the fee(s) have already been paid, Part B - Fee(s) Transmittal should be completed and returned. If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Box ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: Mail **Mail Stop ISSUE FEE**
Commissioner for Patents
Alexandria, Virginia 22313-1450
Fax (703)746-4000

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 4 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Legibly mark-up with any corrections or use Block 1)

20350 7590 07/17/2003

TOWNSEND AND TOWNSEND AND CREW, LLP
TWO EMBARCADERO CENTER
EIGHTH FLOOR
SAN FRANCISCO, CA 94111-3834

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

Certificate of Mailing or Transmission

I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Box Issue Fee address above, or being facsimile transmitted to the USPTO, on the date indicated below.

(Depositor's name)
(Signature)
(Date)

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nonprovisional	YES	\$650	\$0	\$650	10/17/2003

EXAMINER	ART UNIT	CLASS-SUBCLASS
LEARY, LOUISE N	1654	435-004000

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

- ☐ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.
- ☐ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list (1) the names of up to 3 registered patent attorneys or agents OR, alternatively, (2) the name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

1 _____
2 _____
3 _____

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. Inclusion of assignee data is only appropriate when an assignment has been previously submitted to the USPTO or is being submitted under separate cover. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE

(B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent) ☐ individual ☐ corporation or other private group entity ☐ government

4a. The following fee(s) are enclosed:

- ☐ Issue Fee
- ☐ Publication Fee
- ☐ Advance Order - # of Copies _____

4b. Payment of Fee(s):

- ☐ A check in the amount of the fee(s) is enclosed.
- ☐ Payment by credit card. Form PTO-2038 is attached.
- ☐ The Commissioner is hereby authorized by charge the required fee(s), or credit any overpayment, to Deposit Account Number _____ (enclose an extra copy of this form).

Commissioner for Patents is requested to apply the Issue Fee and Publication Fee (if any) or to re-apply any previously paid issue fee to the application identified above.

(Authorized Signature)

(Date)

NOTE: The Issue Fee and Publication Fee (if required) will not be accepted from anyone other than the applicant; a registered attorney or agent; or the assignee or other party in interest as shown by the records of the United States Patent and Trademark Office.

This collection of information is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, Alexandria, Virginia 22313-1450. **DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, Alexandria, Virginia 22313-1450.**

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

TRANSMIT THIS FORM WITH FEE(S)



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TOWNSEND AND TOWNSEND AND CREW, LLP TWO EMBARCADERO CENTER EIGHTH FLOOR SAN FRANCISCO, CA 94111-3834 UNITED STATES				
			EXAMINER LEARY, LOUISE N	
			ART UNIT 1654	PAPER NUMBER

DATE MAILED: 07/17/2003

Determination of Patent Term Extension under 35 U.S.C. 154 (b) (application filed after June 7, 1995 but prior to May 29, 2000)

The patent term extension is 0 days. Any patent to issue from the above identified application will include an indication of the 0 day extension on the front page.

If a continued prosecution application (CPA) was filed in the above-identified application, the filing date that determines patent term extension is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) system. (<http://pair.uspto.gov>)

Any questions regarding the patent term extension or adjustment determination should be directed to the Office of Patent Legal Administration at (703)305-1383.



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			EXAMINER LEARY, LOUISE N	
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Notice of Fee Increase on January 1, 2003

If a reply to a "Notice of Allowance and Fee(s) Due" is filed in the Office on or after January 1, 2003, then the amount due will be higher than that set forth in the "Notice of Allowance and Fee(s) Due" since there will be an increase in fees effective on January 1, 2003. See Revision of Patent and Trademark Fees for Fiscal Year 2003; Final Rule, 67 Fed. Reg. 70847, 70849 (November 27, 2002).

The current fee schedule is accessible from: <http://www.uspto.gov/main/howtofees.htm>.

If the issue fee paid is the amount shown on the "Notice of Allowance and Fee(s) Due," but not the correct amount in view of the fee increase, a "Notice to Pay Balance of Issue Fee" will be mailed to applicant. In order to avoid processing delays associated with mailing of a "Notice to Pay Balance of Issue Fee," if the response to the Notice of Allowance and Fee(s) due form is to be filed on or after January 1, 2003 (or mailed with a certificate of mailing on or after January 1, 2003), the issue fee paid should be the fee that is required at the time the fee is paid. If the issue fee was previously paid, and the response to the "Notice of Allowance and Fee(s) Due" includes a request to apply a previously-paid issue fee to the issue fee now due, then the difference between the issue fee amount at the time the response is filed and the previously paid issue fee should be paid. See Manual of Patent Examining Procedure, Section 1308.01 (Eighth Edition, August 2001).

Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at (703) 305-8283.

Notice of Allowability

Application No.

09/553,424

Examiner

Louise N. Leary

Applicant(s)

SCHNEIDER, LUKE V.

Art Unit

1654

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to election dated 4-28-2003.
2. ☒ The allowed claim(s) is/are 1-38.
3. ☐ The drawings filed on _____ are accepted by the Examiner.
4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) ☐ All b) ☐ Some* c) ☐ None of the:
 1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

* Certified copies not received: _____.
5. ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
 - (a) ☐ The translation of the foreign language provisional application has been received.
6. ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application. **THIS THREE-MONTH PERIOD IS NOT EXTENDABLE**

7. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
8. ☒ CORRECTED DRAWINGS must be submitted.
 - (a) ☒ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
 - 1) ☒ hereto or 2) ☐ to Paper No. 10.
 - (b) ☐ including changes required by the proposed drawing correction filed _____, which has been approved by the Examiner.
 - (c) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No. _____.


Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet.

9. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

- 1 ☒ Notice of References Cited (PTO-892) ✓
- 3 ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948) ✓
- 5 ☒ Information Disclosure Statements (PTO-1449), Paper No. 7.
- 7 ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material

- 2 ☐ Notice of Informal Patent Application (PTO-152)
- 4 ☒ Interview Summary (PTO-413), Paper No. 10.
- 6 ☐ Examiner's Amendment/Comment
- 8 ☒ Examiner's Statement of Reasons for Allowance
- 9 ☐ Other


LOUISE N. LEARY
PRIMARY EXAMINER

1. The following is an examiner's statement of reasons for allowance:

The reasons for allowance of the claims is that none of the prior art of record disclose or suggest (A) a method for analyzing metabolic pathways comprising the steps of (i) administering to a subject a substrate labeled with a stable isotope wherein the abundance of isotope in the substrate is known, (ii) allowing the labeled substrate to be at least partially metabolized by the subject, and (iii) determining the abundance of the isotope in a plurality of target analytes in a sample from the subject to determine a value for the flux of each target analyte, wherein the plurality of target analytes comprise the substrate and/or one or more target metabolites; (B) a method for analyzing metabolic pathways comprising the steps of (i) separating at least partially a plurality of target analytes from biological components contained in a sample obtained from a subject wherein the target analytes comprises a substrate labeled with a stable isotope and/or one or more target metabolites resulting from the metabolism of the substrate by the subject and wherein the relative isotopic abundance of the isotope in the substrate is known and (ii) determining the abundance of the isotope in a plurality of the target analytes in the sample to determine a value for the flux of each target analyte; (C) a method for screening metabolites correlated with a disease comprising the steps of (i) administering to a test subject and a control subject a substrate labeled with a stable isotope wherein the isotopic abundance of the isotope in the substrate is known and the test subject has the disease , (ii) allowing the labeled substrate to be partially metabolized by the test subject and control subject to form one or more target metabolites and wherein the conditions under which the administering and allowing

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steps are performed the same for the test subject and control subject, (iii) obtaining a sample from the test and control subject, (iv) determining the relative abundance of isotope for in a plurality of target analytes for each sample to determine a flux value of each target analyte, and (v) comparing the values for flux for the test and control subjects, a difference in the flux value for a target analyte in the test subject and corresponding flux value for the control subject indicating that such analyte is potentially correlated with the disease; (D) a method for screening for metabolites correlated with a disease comprising the steps of (i) analyzing a sample from a test subject having the disease wherein the sample comprises a substrate labeled with a stable isotope administered to the test subject and/or one or more target metabolites resulting from metabolism of the substrate by the test subject, the relative isotopic abundance of the isotope in the substrate known at the time of administration, and whereby the analyzing step comprises determining the isotopic abundance of the isotope in a plurality of analytes in the sample to determine a value for the flux of each analyte, wherein the plurality of analytes comprise the substrate and/or one or more of the target metabolites; and (ii) comparing flux values for the analytes with flux values for the same analytes obtained for a control subject, wherein a difference in a flux value for an analyte indicates that the analyte is correlated with the disease; (E) a method for screening for the presence of a disease comprising the steps of (i) administering to a test subject a substrate labeled with a stable isotope, wherein the relative abundance of the isotope in the substrate is known, (ii) allowing sufficient time for the labeled substrate to be at least partially metabolized by the test subject to form one or more

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target metabolites known to be correlated with the disease, (iii) performing a plurality of electrophoretic methods in series to at least partially separate a plurality of target analytes from other biological components in a sample obtained from the test subject, wherein the target analytes comprise the substrate and/or one or more of the target metabolites, (iv) determining a flux value for the target analytes wherein the flux value for each target analyte being determined from the abundance of the isotope in that analyte, and (v) comparing determined flux values with corresponding reference flux values for the same target analytes to assess the test subject's risk of disease; (F) a method for screening for the presence of a disease comprising the steps of (i) analyzing a sample from a test subject which comprises a substrate labeled with a stable isotope administered to the test subject and/or one or more target metabolites resulting from metabolism of the substrate by the test subject, the relative isotopic abundance of the isotope in the substrate known at the time of administration and whereby the analyzing step comprises determining the abundance of the isotope in a plurality of analytes in the sample to determine a value for the flux of each analyte, wherein the plurality of analytes comprise the substrate and/or one or more of the target metabolites, and (ii) for each target analyte, comparing the determined flux value with a range of flux values for that analyte wherein the range known to be correlated with the disease and a determined flux value for a target analyte falling within the range for that target analyte indicates that the test subject has the disease or is susceptible to the disease; nor (G) a method for analyzing metabolites in an initial sample comprising the steps of (i) performing a plurality of capillary electrophoresis methods in series comprising

electrophoresing a sample containing multiple metabolites whereby a plurality of resolved metabolites are obtained and wherein (a) the sample electrophoresed contains only a subset of the plurality of resolved metabolites from the immediately preceding method in the series, except the first method of the series in which the sample is the initial sample, the metabolites in the initial sample potentially containing one or more target analytes, (b) the capillary electrophoresis methods are selected from the group consisting of capillary isoelectric focusing electrophoresis, capillary zone electrophoresis and capillary gel electrophoresis and (c) analyzing fractions containing resolved metabolites from the final electrophoretic method to detect the presence of the target analytes as claimed in the present invention.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."


2. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louise N. Leary whose telephone number is (703) 308-3533. The examiner can normally be reached on Monday to Friday from 9:30 to 6 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback, can be reached on (703) 306-3220. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4556.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

For 24 hour access to patent application information, 7 days a week, or for filing patent applications electronically, please visit our website at www.uspto.gov and click on the button "Patent Electronic Business Center" for more information.



LOUISE N. LEARY
PRIMARY EXAMINER

July 16, 2003